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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/697,028	10/25/2000	Jeffrey Olson	11926-112001	3430
26161	7590	02/08/2006	EXAMINER	
FISH & RICHARDSON PC			CHUNDURU, SURYAPRABHA	
P.O. BOX 1022			ART UNIT	PAPER NUMBER
MINNEAPOLIS, MN 55440-1022			1637	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/697,028	Applicant(s) OLSON ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' response to the office action filed on November 29, 2005 has been entered and acknowledged.

Status of the Application

2. Claims 10-16 are pending. Claims 1-9 are cancelled. Applicants' response to the office action is fully considered. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. This action is made FINAL.

3. The following rejection is made in the previous office action:

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Whitcombe et al. (USPN. 6,326,145).

Whitcombe et al. teach a method of claim 1, 16, for biasing (enriching desired nucleic acid) a DNA amplification reaction such that a first nucleic acid having a first nucleotide present at a polymorphic site (allele 1) is amplified to a greater extent than a second nucleic acid having a second, different nucleotide present at the polymorphic site (allele 2) (see col. 12, line 54-67, col. 13, line 1-52), said method comprising (a) contacting a sample of DNA with two amplification primers that hybridize to both the first and second nucleic acid molecule at

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locations that flank the polymorphic site, such that neither the first nor the second primer hybridizes to the polymorphic site (see col. 12, line 54-67, col. 13, line 1-20, col. 12, line 6-20, fig. 11 and 13, indicating opposing primers forward and reverse primers that flank a target sequence); one of the two primers including a 5' portion which, when incorporated into an amplification product, will upon further amplification yield products that form a stable-stem-loop structure (see col. 7, line 49-67, col. 8, line 1-11, col. 9, line 2-24, indicate stem-loop structures formed when scorpion primers are used, Figs. 9, 11-12, indicating stem loop structures), the stem of which is perfectly matched and includes the polymorphic site only when the second nucleotide is present at polymorphic site (allele-specific) (see col. 9, line 2-24, col. 10, line 53-67, col. 11, line 1-17, col. 13, line 45-52);

(b) carrying out amplification, whereby the first nucleic acid molecule is amplified to a greater extent than a second nucleic acid molecule (see col. 13, line 15-63, col. 16, line 20-34).

With regard to claim 16, Whitcombe et al. teach step (c) determining the nucleotide sequence of at least a portion of the DNA present in the amplified DNA sample (see col. 13, line 45-63);

With regard to claims 11-12, 14-15, Whitcombe et al. teach that the DNA comprises single-stranded or double-stranded derived from mammalian (human cells) such as blood, bacteriophage, viruses (see col. 6, line 1-10);

With regard to claim 13, Whitcombe et al. teach that the method further comprises separately carrying out steps (a) and (b) for each of a plurality of polymorphic sites (see col. 10, line 53-59, indicating two-tube (plurality) ARMS test). Accordingly Whitcombe et al. meets the limitations in the instant claims.

Response to Arguments:

4. Applicant's arguments filed on November 28, 2005 have been fully considered but they are not persuasive. Applicant's argue that the prior art reference (USPN. 6,326,145, ('145)) does not anticipate the instant claims. Applicants' argue that the example 1 of the '145 patent cited by the examiner in the rejection, and the Fig. 13 of the patent disclose a probe (scorpion probe) that serves as a means for detecting a nucleic acid molecule and the fluorescence signal produced by probe that matched the target allele increased as the PCR amplification reaction increased the amount of template DNA in the reaction. Applicants further argue that Example 1 of the patent '145 does not disclose differential amplification or do not suggest that two alleles were present in the reaction in Example 1. Applicants' arguments are fully considered and found unpersuasive. First, the patent '145 is mainly concerned with scorpion primers which are capable of forming hairpin loops when incorporated into the amplification product (see at least col. 11, line 1-12, where the primers are used as probes). Second, the example 1 does teach the use of scorpion primers for allele discrimination (see col. 12, line 54-59, which clearly indicates hairpin forming regions of the primers and the probes are used in quantitating the alleles (normal Vs mutant allele) in a real-time PCR format. Thus the Example 1 clearly indicates or suggests two alleles (normal and mutant allele) and does indicate the incorporation of scorpion primers into the amplicon that are detected by the probes targeted to these alleles. Fig 11 of the patent '145 shows scorpion primers in allele discrimination and Fig 12 and 13 shows detection system involving a probe in monitoring amplification in a real-time PCR format. Thus the patent '145 does disclose differential amplification. In addition, the instant claims are in "comprising" open language

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format and thus any additional step can be added. Thus the claims do not exclude the real-time PCR format of monitoring amplification reaction using detection probe signals.

Applicants' also argue that the stem-loop formed by the '145 probe is for detection and not for differential amplification and argue that the scorpion probe includes a FRET signaling system, wherein the probe comprises a fluorophore and a quencher and extension of scorpion probe on to the target will cause the incorporation into probe of additional sequence and depending on the complementarity of the probe with the target, the stem-loop form. Applicants' also argue that the example 2 of the '145 patent and Fig 14 indicates the use of two different scorpion probes and argue that probes were causing the differential amplification and the efficiency of the amplification would depend on the match/ mismatch probe used. Applicants' arguments are fully considered and found unpersuasive. Examiner agrees that the scorpion probes are used in detection system, however, the probe alone does not constitute the amplification reaction. The '145 patent' main invention is drawn to novel scorpion primers and their use in PCR. Examiner reiterates that the '145 patent also teach that the primers are used as probes in allele discrimination (see col. 11, line 1-12). The scorpion primers used in Example 1 does incorporate into the amplicon and the detection of said primer extension products are monitored in a real-time situation using probes that match/mismatch said alleles. Thus primer incorporation and probe hybridization is a simultaneous process in the real-time PCR system. Thus the fluorescence signal is monitored as an indication of the presence or absence of the target in the sample in a quantitative way, where that signal is proportional to the amount of the target present in the sample. Therefore the '145 patent does disclose differential amplification does disclose monitoring said amplification using probe(s) in a real-time PCR format.

Further Applicants argue that the scorpion probes are not fully incorporated into the amplification product, because said probes include a blocking moiety that prevents tail region and argue that the probes do not contain a 5' region that is incorporated into the amplification as required by the patent claims and argue that the '145 patent discloses just opposite to the instant method of invention. Applicants' arguments are full considered and found not persuasive. The arguments regarding a blocking moiety are irrelevant to the present context, because first, the instant claims do not recite use of a probe with a 5' - tail region, second Applicants' bring yet another portion of the '145 patent (col. 5, line 51-65) that discloses amplification processes using the primer of the invention, and not a probe with a tail region as asserted by the applicants. Examiner also notes that the cited paragraph supports the anticipation of the claims, because the cited paragraph suggests the use of scorpion primers of the invention in reverse transcription and also in other amplification techniques such as SDA, NASBA, SDA etc. Therefore the arguments are irrelevant to the present context and the disclosure of '145 patent does anticipate the instant claims. Therefore the rejection is maintained.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period


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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Suryaprabha Chunduru 2/6/06
Patent Examiner
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